

RDCRN: *A Model for Collaborative Rare Diseases Research Efforts*

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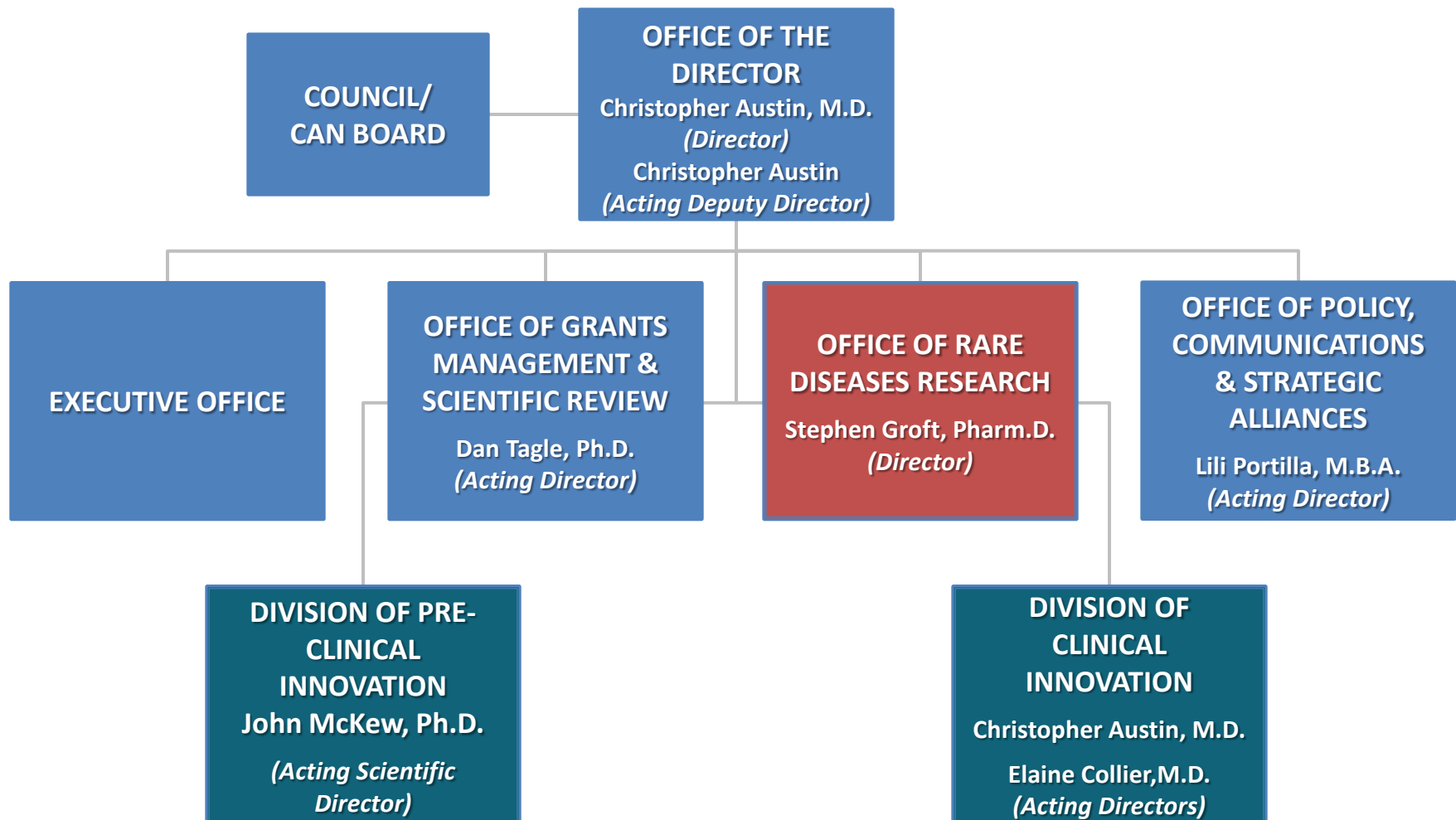
GENE THERAPY: CHARTING A FUTURE COURSE

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NIH, BETHESDA

NCATS

National Center for Advancing Translational Sciences (NCATS)



Office of Rare Diseases Research (ORDR), NCATS Collaborative Programs

Stimulates and coordinates research on rare diseases

- **Rare Diseases Clinical Research Network (RDCRN)**
- Scientific Conferences
- NIH Clinical Center Bench to Bedside Research Program with Intramural/Extramural Research Investigators partnership

Rare Diseases: Background

- Prevalence < 200,000 people in the USA
- Estimated 6%-8% of Population has a Rare Disease
- > 7000 Genetic and Acquired Rare Diseases
- ~ 18-25 million people in the United States are affected
- Exact Prevalence Unknown
- Global Distribution of Patients

Challenges for Rare Diseases Research

- Disease often not well characterized or defined
- Rarity means:
 - Recruitment for clinical studies is usually quite difficult
 - Study populations become widely dispersed
 - Few expert centers for diagnosis, management, and research
- Often little high-quality evidence available to guide treatment

The Rare Diseases Clinical Research Network (RDCRN)

NCATS

1) RDCRN (Background)

To facilitate clinical research

- Established in 2003: by the Office of Rare Diseases Research, six NIH Institutes & Centers (ICs) collaborated: 10 Rare Diseases Clinical Research Consortia (RDCRC) and 1 Data Management Coordinating Center (DMCC)
- Expanded in 2009: initially to 19 RDCRC and 1 DMCC (eight collaborating ICs)
- Each RDCRC : multiple diseases/ investigators / sites collaborative clinical research Involving Patient Advocacy Groups (PAGs)
- Cooperative agreement (U54) awards for 5 years
- 3rd cycle in planning stage
 - Renewal is planned- open competition

Goals of the RDCRN

- Facilitate clinical research by:
 - Creating multi-site Consortia focused on minimum three related diseases
 - Making meaningful large-scale clinical studies possible
 - Longitudinal studies, pilot projects and Clinical Trials, Natural History Studies are required)
 - Establishing uniform protocols for data collection
 - Cost sharing infrastructure
- Collaborate with patients advocacy groups (as research partners)
- Train new investigators
- Provide Website resource for education and research in rare diseases

Requirements for each RDCRC

- Two clinical studies (one longitudinal study, 2nd can be a clinical trial)
- Pilot projects program
- Career development program (training of investigators)
- Collaboration with PAGs
- Collaboration with DMCC and NIH scientific staff

About the RDCRN

- 225 clinical sites world-wide, collectively studying more than 200 diseases
- 17 Consortia & DMCC
- 86 Accruing protocols
 - 17188 patients enrolled in studies
 - Natural History studies, clinical trials, Genotype/Phenotype
- 2,290 consortium members
- 95+ patient advocacy groups
- 174 trainees

RDCRN is supported by

- ORDR/NCATS
- NINDS
- NICHD
- NIDDK
- NIAID
- NIDCR
- NIAMS
- NHLBI
- NCI

DHHS-NIH
ORDR/NCATS, NINDS,
NIAMS, NICHD, NHLBI,
NIDDK, NIDCR, NIAID, NCI

**Coalition of Patient
Advocacy Groups
(CPAG)**

**Chronic Graft Versus
Host Disease Consortium**

**North America Mitochondrial
Diseases Consortium**

**Primary Immune Deficiency
Treatment Consortium**

**The Data Management
and Coordinating
Center**

**Rare Kidney
Stone Consortium**

**Nephrotic Syndrome
Rare Disease Clinical
Research Network**

**Angelman, Rett and
Prader-Willi Syndromes
Consortium**

**Brain Vascular
Malformation Consortium**

**Autonomic Rare Diseases
Clinical Research Consortium**

**Sterol and Isoprenoid
Diseases Consortium**

**Salivary
Gland Carcinomas Consortium**

**Urea Cycle Disorders
Consortium**

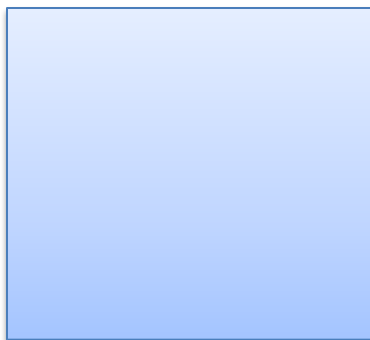
**Inherited Neuropathies
Consortium**

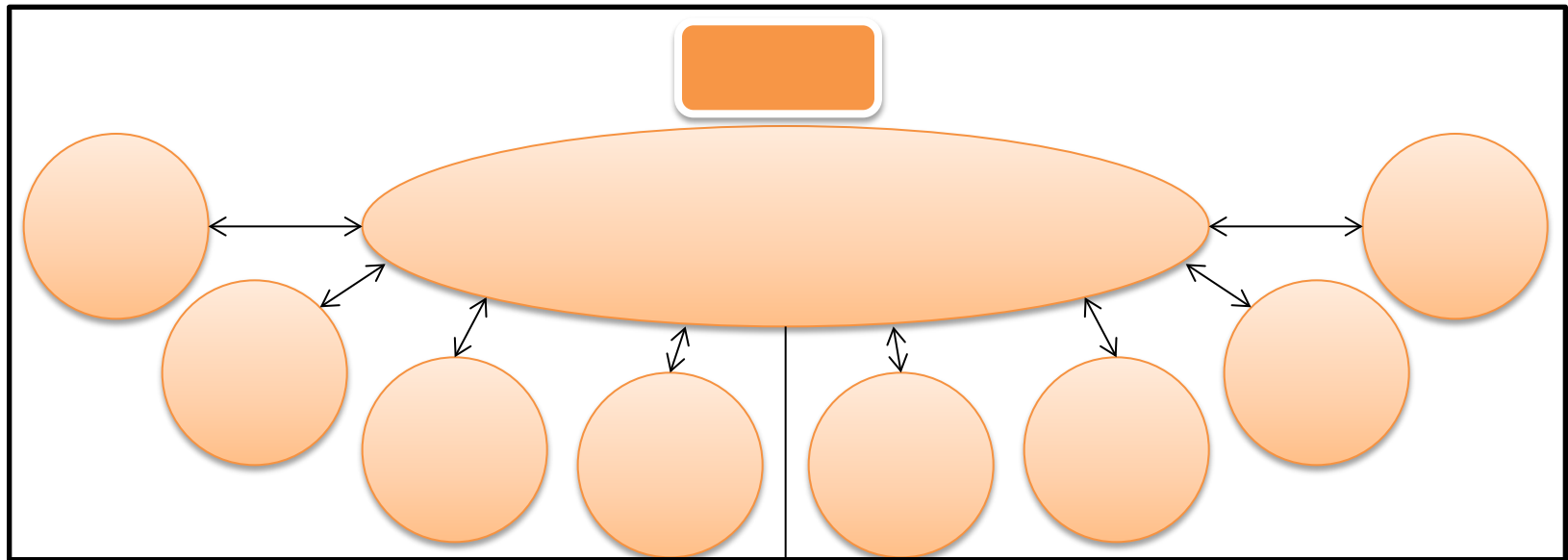
**Lysosomal
Disease Network**

**Vasculitis Clinical
Research Consortium**

**Porphyria Rare Disease
Clinical Research Consortium**

**Genetic Disorders of Mucociliary
Clearance Consortium**





	Genetic Disorder of Mucociliary Clearance	Porphyrias	Urea Cycle Disorders
Autonomic Rare Diseases			Vasculitis
Brain Vascular Malformation		Rare Kidney Stone	DMCC
	NEPTUNE: Nephrotic Syndrome	Salivary Gland Carcinomas	> 95 PAGs (CPAG)
Dystonia Coalition	North American Mitochondrial Diseases	STAIR: Sterol and Isoprenoid Diseases	

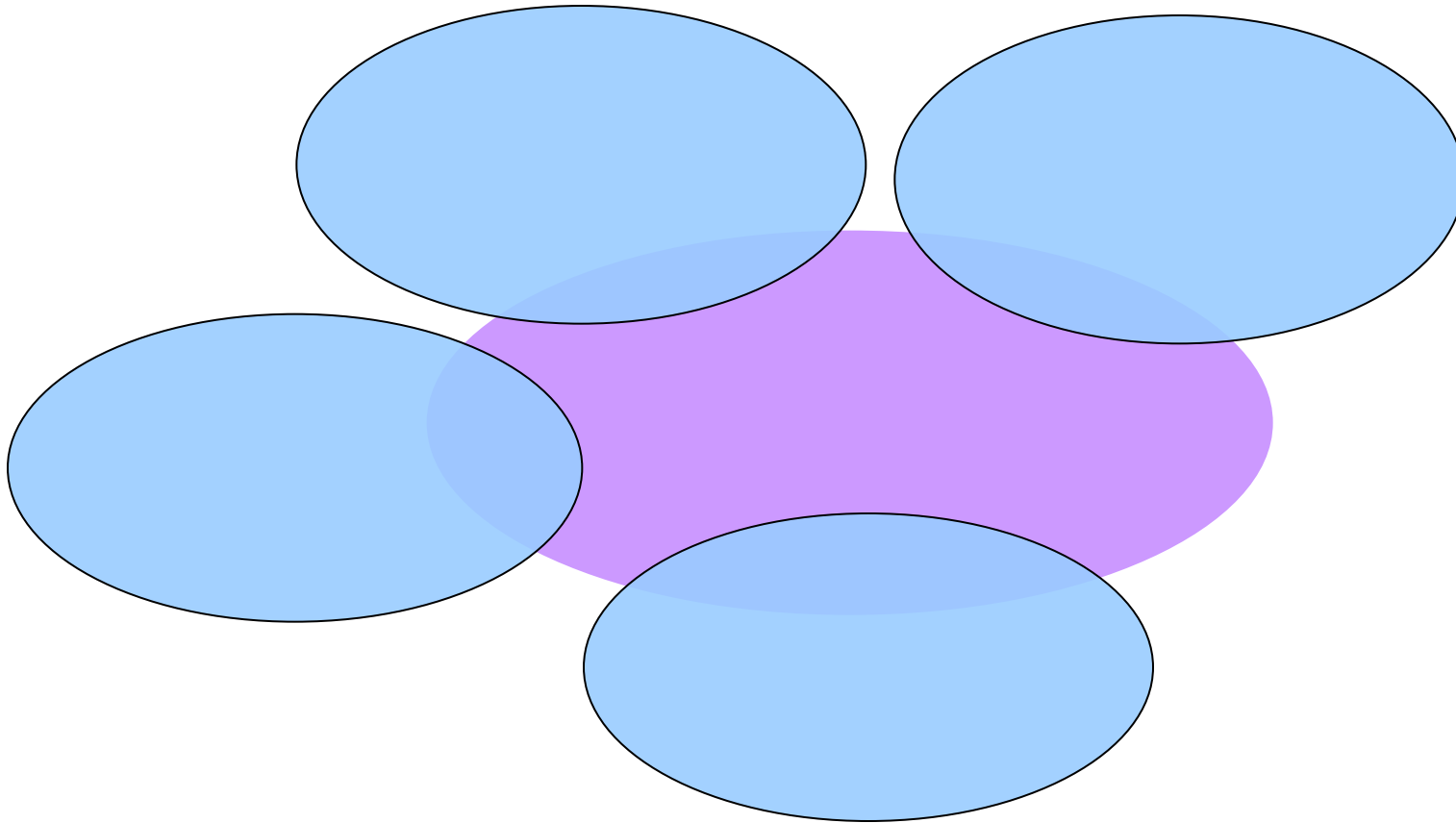
Value of PAGs as Research Partners

Since 2004 Many PAGs within RDCRN are involved in more than one of the following expanded roles as research partners-

- Recruit patients for clinical studies, encourage participation in NHS
- Identify cohorts of patients with range of phenotypic expression
- Provide financial support for research and training programs of RDCRC (consortia) and patient registries
- Educate patients, public, media and health care providers
- Identify research efforts and translate research results to communities
- Organize and fund research based Scientific conferences and meetings for patients/families/caregivers
- Provide financial support for *travel clinics* to facilitate patient access to investigators and studies
- Establish global partnership

RDCRN Steering Committee Organization

Review, facilitate and establish all Network procedures and functions



RDCRN Protocols

Type of Study	Number of Protocols	DMCC Forms	DMCC Specimen System	DMCC Pharmacy System
Pilot	8	8	3	5
Longitudinal	67	54	15	0
Phase I	2	2	0	2
Phase II	7	7	2	7
Phase III	4	3	0	2
IND	5	5	1	3
Industry Sponsored	5	5	3	4
Case Control	2	1	0	0
Chart Review	1	0	0	0

RDCRN U.S. Sites

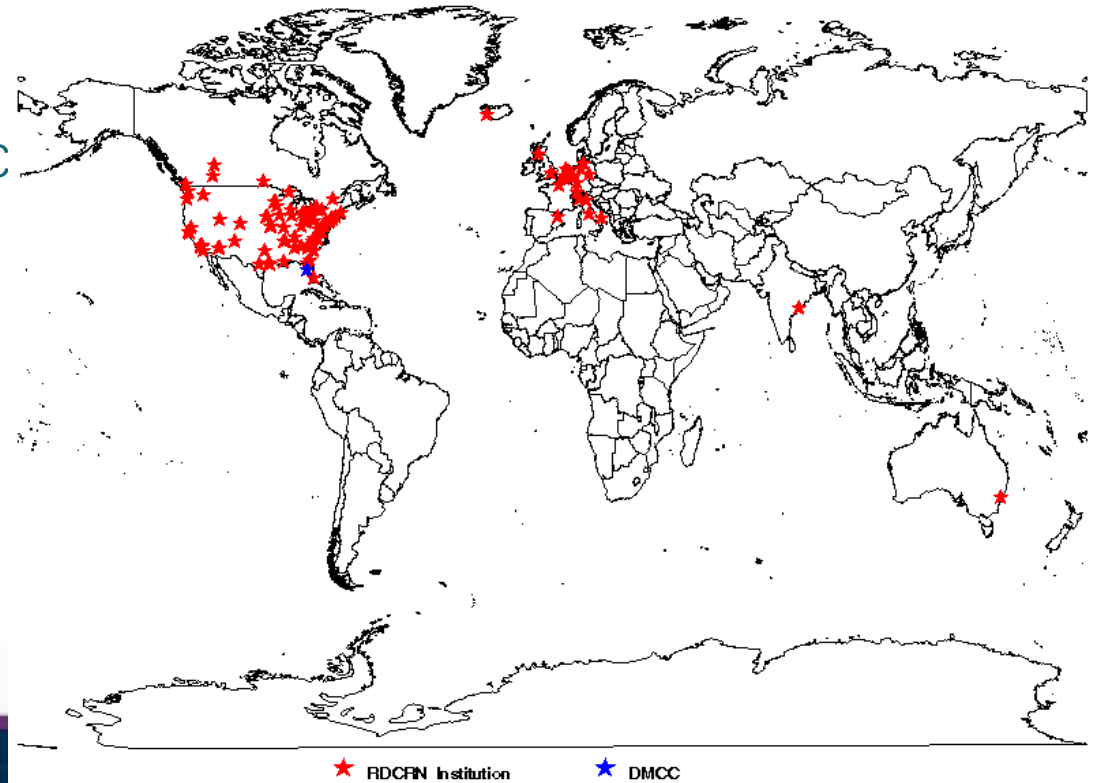


★ RDCRN Institution

★ DMCC

RDCRN International Sites

- Australia (INC)
- Belgium (DC)
- Canada (BVMC, DC, LDN, MCC, NAMDC, NEPTUNE, PIDTC, RKSC, STAIR, UCDC, VCRC)
- England (DC, INC)
- France (DC, RKSC)
- Germany (DC, INC, RKSC, UCDC)
- Iceland (RKSC)
- India (DC)
- Italy (DC, INC, RKSC)
- Netherlands (DC, RKSC)
- Scotland (DC)
- Spain (RKSC)
- Switzerland (UCDC)



RDCRN Data Management and Coordinating Center (DMCC)

- Supports RDCRN by providing technologies, tools to collect clinical research data and support of study design and data analysis
- On-line protocol management system
 - Web-based patient enrollment (recruitment and referral)
 - Data entry and collection with data standards
 - Adverse event reporting
- Provides protocol training for research staff
- Works with the individual NIH Institutes' Data and Safety Monitoring Boards to establish protocols for Adverse Events notification and reporting

Responsibilities of DMCC (Cont.)

- Monitor Network protocol adherence, data collection and data submission
- Coordinates site visits for auditing individual consortia sites
- Provides a user-friendly web resource site for the public, research scientists, and clinicians; involvement of PAGs
- Maintain members' website, documentation and database
- Oversees and maintains RDCRN Patient Contact Registry

Are YOU Interested In Research On Rare Diseases?

Have study information sent right to your inbox!



Receive the most current information on:

- open recruitment for clinical studies of your disease
- opening of new clinical sites doing research on rare diseases
- activities from affiliated awareness and advocacy groups

...and future opportunities to participate in research!

YOU can help in the fight against rare diseases

[Register Today!](#)

RDCRN Clinical Studies

Maintaining the Relationship Between Patients and Researchers is Vital!

Participation in Research Makes it Possible for Researchers to:

- provide the best possible care to patients affected by rare diseases
- improve methods in studying your disease
- achieve deeper understanding of your disease and its causes
- find new treatments
- create new studies

The RDCRN has over 150 clinical sites available, and is adding more every day! [View All Studies](#)

Spotlight On Rare Diseases

Spotlight

Quarterly Newsletter of the NIH Rare Diseases Clinical Research Network

Save The Date: October 2, 2012



Network Resources



Who Are We?

The Rare Diseases Clinical Research Network (RDCRN) is made up of 18 distinctive consortia that are working in concert to improve availability of rare disease information, treatment, clinical studies, and general awareness for both patients and the medical community. The RDCRN also aims to provide up-to-date information for patients and to assist in connecting patients with advocacy groups, expert doctors, and clinical research opportunities.

Click on the Consortium Name to view the diseases or disorders studied by each consortium. Clicking on a disease or disorder name will take you directly to a description of that disease or disorder.

[N] Angelman, Rett, and Prader-Willi Syndromes Consortium Go To Web Site Study Information	[N] HEPTUNE: Hepatobiliary Syndrome Rare Disease Clinical Research Network Go To Web Site Study Information
[N] Autonomic Rare Diseases Clinical Research Consortium Go To Web Site Study Information	[N] North American Mitochondrial Diseases Consortium Go To Web Site Study Information
[N] Brain Vascular Malformation Consortium Go To Web Site Study Information	[N] Porphyrias Consortium Go To Web Site Study Information
[N] Chronic Graft Versus Host Disease Consortium (COVHD) Go To Web Site Study Information	[N] Primary Immune Deficiency Treatment Consortium Go To Web Site Study Information
[N] Dystonia Coalition Go To Web Site Study Information	[N] Rare Kidney Stone Consortium Go To Web Site
[N] Genetic Disorders Of Mucociliary Clearance Go To Web Site Study Information	[N] Salivary Gland Carcinomas Consortium Go To Web Site Study Information
[N] Inherited Neuropathies Consortium Go To Web Site Study Information	[N] RANK: Rare And Inherited Disorders Consortium Go To Web Site Study Information
[N] Lyonssomal Disease Network Consortium Information Study Information	[N] Time Cycle Disorders Consortium Go To Web Site Study Information
	[N] Vasculitis Clinical Research Consortium Go To Web Site Study Information

Former Partners of the Rare Diseases Clinical Research Network

[N] Bone Marrow Failure Consortium (BMFC) Contact This Consortium More Information	[N] Rare Genetic Steroid Disorders Consortium (RGSDC) Contact This Consortium More Information
[N] Cholestatic Liver Disease Consortium (CLDC) Go To Web Site Contact This Consortium More Information	[N] Rare Lung Diseases Consortium (RLDC) Go To Web Site Contact This Consortium More Information
[N] CRICH: Clinical Investigation Of Neurologic Challenges Go To Web Site Contact This Consortium More Information	[N] Rare Thrombotic Diseases Consortium (RTDC) Go To Web Site Contact This Consortium More Information
[N] Clinical Research Consortium For Spinocelebellar Ataxias More Information	

ABOUT THE RDCRN

The Rare Diseases Clinical Research Network (RDCRN) is funded by the National Institutes of Health (NIH) and the Office for Rare Diseases Research (ORDR). RDCRN was created to facilitate collaboration among experts in many different types of rare diseases. Our goal is to contribute to the research and treatment of rare diseases by working together to identify biomarkers for disease risk, disease severity and etiology, and clinical outcomes, while also encouraging development of new approaches to diagnosis, prevention, and treatment. [More About the RDCRN](#)

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Contact Web Master | Accessibility | Disclaimer



RDCRN Website

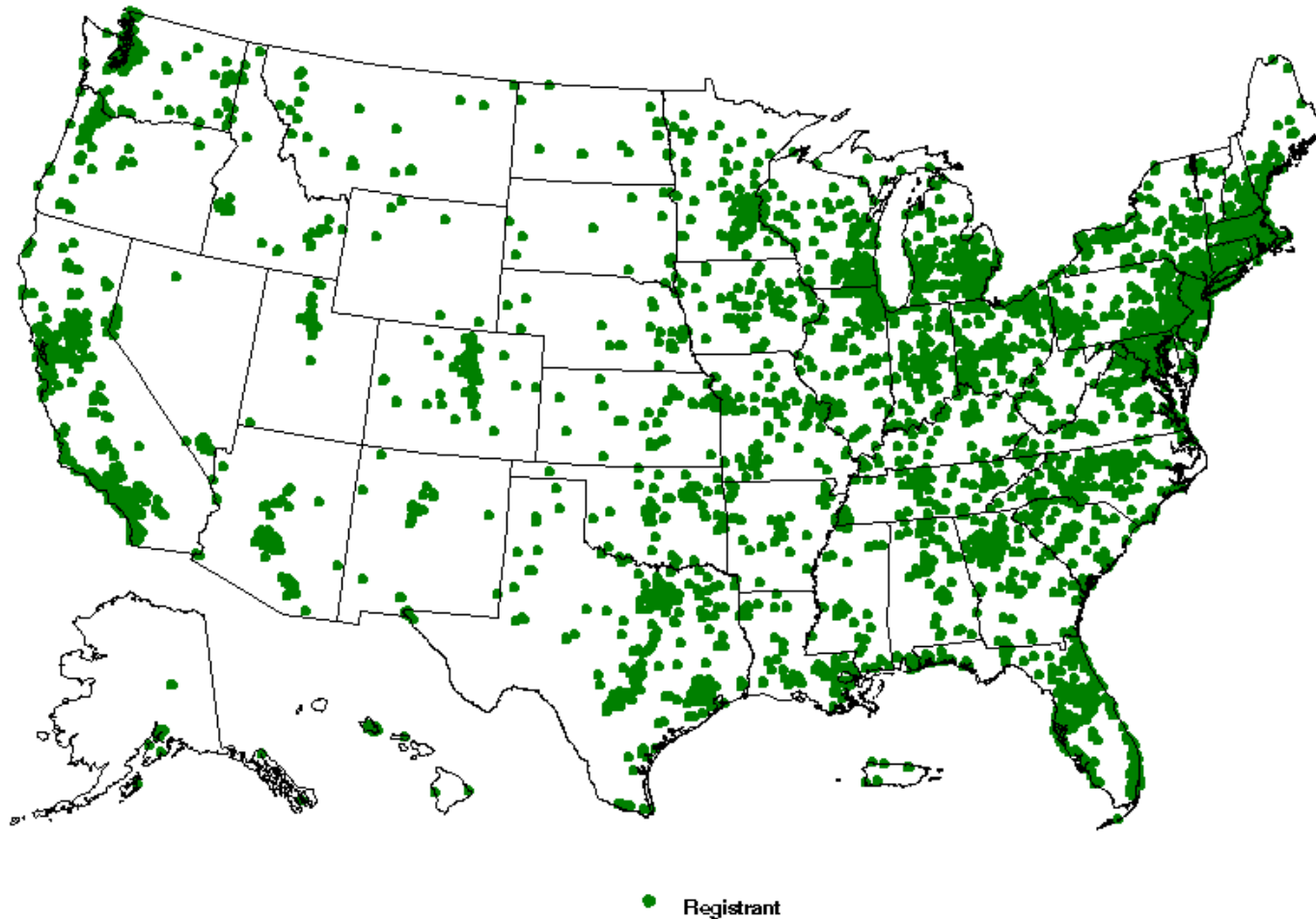
<http://rarediseasesnetwork.org>

- Portal to websites for each Consortium
 - *Contact PIs for collaboration*
- Portal to members' website
- Portal for patient advocacy groups
- RDCRN Contact Registry
- RDCRN Media Center

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RDCRN Contact Registry (2004)

(U.S. Geographic Distribution of Contact Registrants)



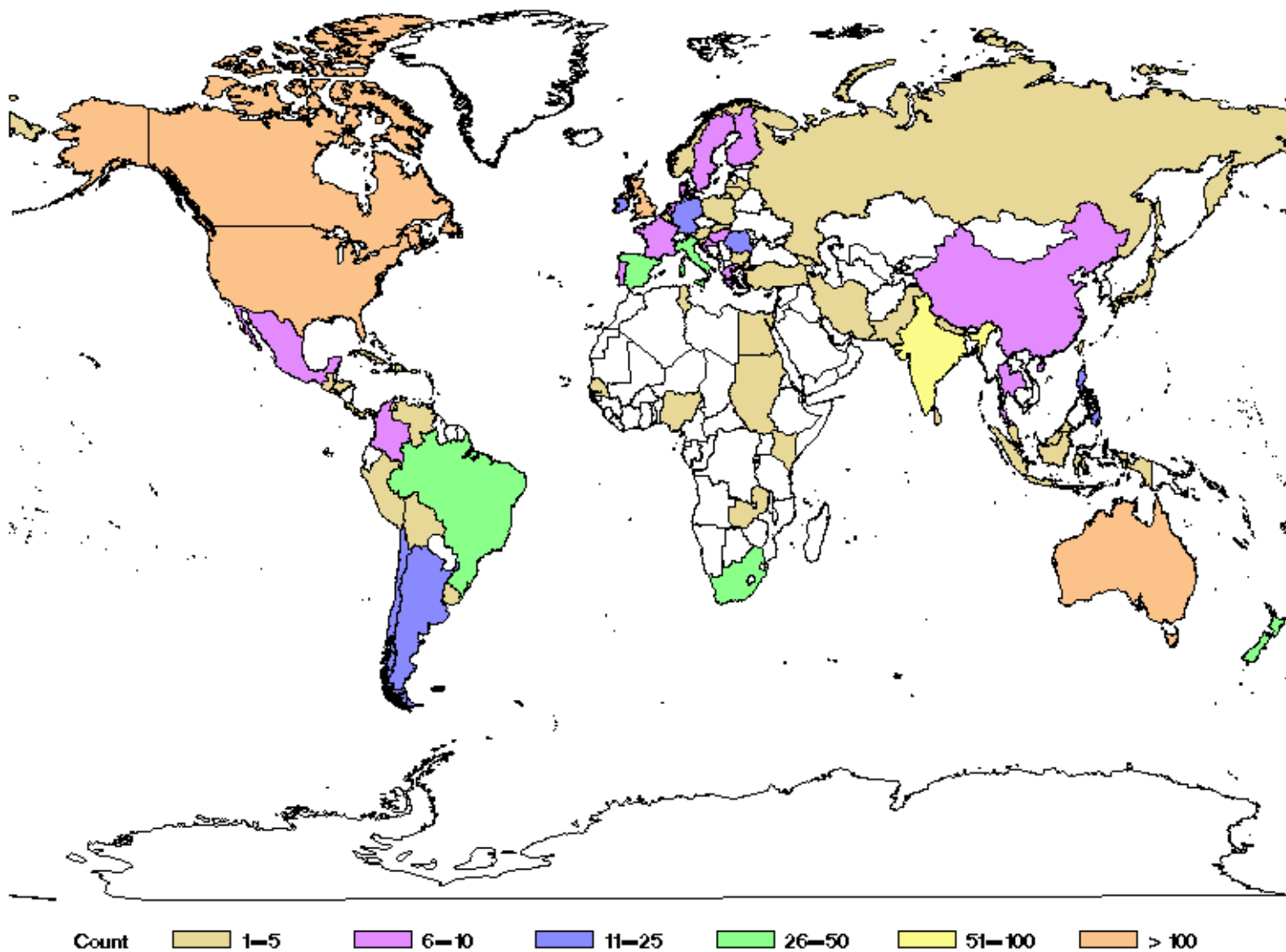
- Enrollment open to patients with diseases under study by Consortia

- Provides international on-line system for communication, recruitment, research

- more than 12000 Registrations

- 180 Diseases represented in 67 countries

World Geographic Distribution of Contact Registrants



Data Sharing and ORDR Datarepository

- The DMCC also coordinates with NIH program staff including registration with and data uploading of appropriate RDCRN studies to ORDR-governed data repository
- Through dbGaP, a database for genotypes and phenotypes (NCBI, National Library of Medicine)
- Data transfer to dbGaP occurs on regular basis
- RDCRN Data Access Committee (DAC)

Urea Cycle Disorders Consortium (PI- Dr. Mark Batshaw)

- They are developing adeno-associated viral gene therapy for *Ornithine Transcarbamylase (OTCD) deficiency* in neonates.
- They have a candidate vector and are ready to move into clinical trials.

Primary Immunodeficiency Treatment Consortium (PI- Mort Cowan)

- 1) Dr. Notarangelo (co-PI of the PIDTC) has an active protocol for gene therapy for XSCID using a lentiviral vector.
 - It's a collaborative study with several other PIDTC institutions in the US as well as in France and the UK.
- 2) The group is doing the pre-clinical studies necessary for an IND for Artemis-deficient SCID (SCID A)

Team Work!

- Clinical Sites
- Principal and co-investigators and The DMCC
- Trainees
- Study Coordinators
- Patient Advocacy Groups (PAGs)
- Pharmaceutical industry
- NIH ORDR and ICs staff (program officers and project scientists)
- Patients

RDCRN: Working model for collaborative, multi-site clinical studies in an inexpensive way!

RDCRN consists of ~225 sites, 97 PAGs and conducts research on 200 rare diseases

RDCRN Request For Applications (RFA)

- Current U54 awards end in 2014
- Plan to reissue the RDCRN RFA
- Timeline - similar to last RFA
- NIH ICs as collaborators

Contact:

- RDCRN: <http://www.rarediseasesnetowrk.epi.usf.edu>
- 2008 RFA: <http://www.rarediseases.info.nih.gov>
- Notice of Intent to publish RDCRN RFA:
<http://grants.nih.gov/grants/guide/notice-files/NOT-TR-13-004.html>
- Program Contact: Rashmi Gopal-Srivastava, Ph. D.
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Turning Discovery Into Health



Thank you for your attention

Contact information: gopalr@mail.nih.gov

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